= SRCH HISTORY =

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> d hist

     (FILE 'HOME' ENTERED AT 17:23:04 ON 30 SEP 2003)

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 17:23:15 ON 30 SEP 2003
L1           195 S (EXPRESSION(3A) PROFILE) AND ALZHEIMER?
L2           197 S (EXPRESSION(3A) PROFILE?) AND ALZHEIMER?
L3           260 S (EXPRESSION(3A) PROFIL?) AND ALZHEIMER?
L4            12 S L3 NOT PY>1997
L5             7 DUP REM L4 (5 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 17:32:15 ON 30 SEP 2003
L6             0 S STAGE? (4A) ALZHEIMER?

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 17:37:48 ON 30 SEP 2003
L7           947 S STAGE? (4A) ALZHEIMER?
L8            76 S L7 AND EXPRESSION
L9            14 S L8 NOT PY>1997
L10            7 DUP REM L9 (7 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 17:41:32 ON 30 SEP 2003

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 17:52:51 ON 30 SEP 2003
L11           12 S MRNA (4A) DETECTION (4A) ALZHEIMER?
L12            8 DUP REM L11 (4 DUPLICATES REMOVED)
L13            2 S L12 NOT PY>1997

     FILE 'STNGUIDE' ENTERED AT 17:55:58 ON 30 SEP 2003

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 18:04:24 ON 30 SEP 2003
L14            0 S L7 AND (ARRAY? OR MICROARRAY?)
L15            0 S L7 (3A) (ARRAY? OR MICROARRAY?)
L16            0 S L7 (7A) (ARRAY? OR MICROARRAY?)
L17          123 S ALZHEIMER? (4A) EXPRESSION (4A) (RNA? OR MRNA?)
L18           61 S L17 NOT PY>1997
L19           43 DUP REM L18 (18 DUPLICATES REMOVED)
L20            0 S L19 AND STAGE
L21       665787 S L19 (3A) PANEL? OR PROFILE?

     FILE 'STNGUIDE' ENTERED AT 18:20:05 ON 30 SEP 2003
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L Number	Hits	Search Text	DB	Time stamp
1	16961	Alzheimer$	USPAT; US-PGPUB	2003/09/30 16:41
2	3003	Alzheimer$ same express$	USPAT; US-PGPUB	2003/09/30 16:41
3	390	Alzheimer$ same express$ same patient	USPAT; US-PGPUB	2003/09/30 16:43
4	811	Alzheimer$ same express$ same patient$	USPAT; US-PGPUB	2003/09/30 16:43
5	3	Alzheimer$ same express$ same patient$ same profile$	USPAT; US-PGPUB	2003/09/30 16:44
7	0	Alzheimer$ same express$ same patient$ same (gene adj profile)	USPAT; US-PGPUB	2003/09/30 16:44
8	109	Alzheimer$ same express$ same patient$ same mRNA$	USPAT; US-PGPUB	2003/09/30 16:58
9	1	wo-8910977-$	USPAT; US-PGPUB; EPO	2003/09/30 17:00
10	0	wo-8910977-$ and alzheimer$	USPAT; US-PGPUB; EPO	2003/09/30 17:02
11	3643	array$ and alzheimer$	USPAT; US-PGPUB; EPO	2003/09/30 17:03
12	888	microarray$ and alzheimer$	USPAT; US-PGPUB; EPO	2003/09/30 17:03
13	107208	DNA array$ and alzheimer$	USPAT; US-PGPUB; EPO	2003/09/30 17:03
14	8646	(DNA array$) and alzheimer$	USPAT; US-PGPUB; EPO	2003/09/30 17:04

09/534,846

L #Number	Hits	Search Text	DB	Time stamp
1	7	array same alzheimer$ same expression	USPAT; EPO	2003/09/30 18:38
3	128	((microarray$ or array$) same alzheimer$) same detect$	USPAT; EPO	2003/09/30 18:39
2	160	(microarray$ or array$) same alzheimer$	USPAT; EPO	2003/09/30 18:39

L5 ANSWER 1 OF 7 MEDLINE on STN DUPLICATE 1

AB In **Alzheimer**'s disease (AD), one cell in the brain may clearly be affected, while an adjacent cell appears healthy or unaffected. Previous technology has allowed us to examine one message at a time, at the level of a single cell (in situ hybridization, ISH), or multiple messages in a heterogeneous population of cells (Northern analysis). We have developed a methodology to build up a **profile** of multiple mRNA **expression** in single, whole, post-mortem cells that have been immunohistochemically (IHC) characterized. Fresh post-mortem tissue is spread into a layer one cell thick and fixed. Neurons are identified using an antibody to neurofilament and isolated using a micropipette. The mRNA is reverse transcribed and PCR carried out to confirm that material is present. A radioactively labeled antisense aRNA probe, which is representative of the messages contained in the cell is then amplified. This aRNA is used as a probe for a reverse Northern blot, allowing us to profile many genes from one cell at the same time. This technology has the potential to be applied to a wide variety of diseases encompassing many different cell types.

ACCESSION NUMBER: 1998066175 MEDLINE
DOCUMENT NUMBER: 98066175 PubMed ID: 9402555
TITLE: Isolation of single immunohistochemically identified whole neuronal cell bodies from post-mortem human brain for simultaneous analysis of multiple gene expression.
AUTHOR: Cheetham J E; Coleman P D; Chow N
CORPORATE SOURCE: Department of Neurobiology and Anatomy, University of Rochester School of Medicine and Dentistry, NY 14623, USA.
CONTRACT NUMBER: AG08665 (NIA)
AG09016 (NIA)
RO1 AG01121 (NIA)
SOURCE: JOURNAL OF NEUROSCIENCE METHODS, (1997 Nov 7) 77 (1) 43-8.
Journal code: 7905558. ISSN: 0165-0270.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980129

L5 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AB Neuronal thread proteins (NTPs) comprise a family of molecules expressed in brain and primitive neuroectodermal tumor cell lines. In **Alzheimer**'s disease (AD). increased CNS levels of the 21 kD NTP species are correlated with dementia. The present study characterizes the nature and distribution of NTP expression using recently generated brain-derived polyclonal and monoclonal antibodies (MoAbs) to recombinant AD7c-NTP protein. In AD, high levels of NTT gt immunoreactivity were detected in neuronal perikarya, neuropil fibers, and white matter fibers (axons). In addition, 4 of the 23 AD7c-NTP MoAbs labeled degenerating neurons (with or without neurofibrillary tangles), axonal spheroids, dystrophic neurites, or irregular, wavy threadlike neuropil fibers in AD. Increased neuronal AD7c-NTP immunoreactivity in AD colocalized with perikaryal accumulations of tau-1, phosphorylated neuronal lament, and the ganglioside, A2B5. In addition, AD7c-NTP immunoreactivity was detected in early neuritic plaques along with beta-amyloid-containing fibrils, but not in mature plaques, nor was it colocalized in beta-A4-immunoreactive fibrils. This study demonstrates the profiles of NTP overexpression in relation to paired helical filament-associated neurodegenerative lesions in AD.

ACCESSION NUMBER: 1996:527643 BIOSIS
DOCUMENT NUMBER: PREV199699249999
TITLE: Profiles of neuronal thread protein expression in **Alzheimer**'s disease.

AUTHOR(S): De La Monte, Suzanne M. (1); Carlson, Rolf I.; Brown, Nancy V.; Wands, Jack R.
CORPORATE SOURCE: (1) MHG Cancer Cent., Room 7308, MGH East, 149 13th St., Charlestown, MA 02129 USA
SOURCE: Journal of Neuropathology & Experimental Neurology, (1996) Vol. 55, No. 10, pp. 1038-1050.
ISSN: 0022-3069.
DOCUMENT TYPE: Article
LANGUAGE: English

L5 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 2
AB Annexins are Ca(2+)-dependent membrane-binding proteins that are potentially important in Ca(2+)-induced neurotoxicity or neuroprotection. To address the possible involvement of annexins in cellular reactions to brain injury and neurodegenerative disease, we studied the immunohistochemical localization of annexins I, II (p36 and p11), IV, and VI in the adult human hippocampus. Formalin-fixed, paraffin-embedded tissue from autopsy cases representing hypoxic-ischemic injury, seizure disorders, **Alzheimer**'s disease, and age-related controls were examined. Neurons showed cytoplasmic immunoreactivity for annexin I, whereas annexin VI was distributed in patterns suggesting plasma membrane and perisynaptic locations. The cytoarchitectural distribution of annexin VI within neurons was altered in pathological states and annexin VI was strongly associated with neuronal granulovacuolar bodies in **Alzheimer**'s disease. Reactive astrocytes expressed annexins I, II (p36 and p11), and IV, whereas quiescent astrocytes were minimally immunoreactive. Significant annexin immunoreactivity was also detected in oligodendrocytes (annexin IV), ependymocytes (I, II, and IV), choroid plexus (I, IV, and VI), meningothelium (I, II, IV, and VI), and vascular endothelium (II and IV) and smooth muscle (I, IV, and VI). This is the first comparative study of immunoreactivities for multiple annexins in human brain. Neurons and glia display selective and different **profiles** of annexin protein **expression** and show immunohistochemical changes in pathological conditions, which suggest involvement of annexins in neuronal and glial reactions to injury.
ACCESSION NUMBER: 94361211 MEDLINE
DOCUMENT NUMBER: 94361211 PubMed ID: 8080046
TITLE: Alterations of annexin expression in pathological neuronal and glial reactions. Immunohistochemical localization of annexins I, II (p36 and p11 subunits), IV, and VI in the human hippocampus.
AUTHOR: Eberhard D A; Brown M D; VandenBerg S R
CORPORATE SOURCE: Department of Pathology (Neuropathology), University of Virginia Health Sciences Center, Charlottesville 22908.
CONTRACT NUMBER: NINCDS T32 NS 7236 (NINDS)
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (1994 Sep) 145 (3) 640-9.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941013
Last Updated on STN: 19980206
Entered Medline: 19941004

L5 ANSWER 4 OF 7 MEDLINE on STN DUPLICATE 3
AB Several forms of **Alzheimer** amyloid precursor protein (APP) mRNA are generated by alternative splicing. Among them, the APP695 mRNA skipping the exon 7 and 8 is expressed specifically in neurons, suggesting that this alternative splicing is regulated in a neuron-specific manner. As the first step for investigating the mechanism of the neuron-specific splicing, a mini-gene system was developed, in which mini-APP genes consisting of the exon 6, 7, 8, 9 and their flanking regions were

introduced into neuronal and nonneuronal cultured cell lines to see their **expression profiles**. In the system the exon 7 and 8 of the mini-gene were significantly skipped in the neuronal cell, and the deletion study indicated that cis-acting elements for skipping the exons existed in the corresponding skipped-exon and its flanking regions. A small deletion upstream of the exon 8 suppressed the skipping of the exon 8 in the neuronal cell, suggesting that one of the regulatory sequence(s) for the exon skipping exists in a small region upstream of the skipped exon.

ACCESSION NUMBER: 93371441 MEDLINE
DOCUMENT NUMBER: 93371441 PubMed ID: 8363619
TITLE: Neuron-specific splicing of the **Alzheimer** amyloid precursor protein gene in a mini-gene system.
AUTHOR: Yamada T; Goto I; Sakaki Y
CORPORATE SOURCE: Department of Neurology, Faculty of Medicine, Kyushu University, Fukuoka, Japan.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1993 Aug 31) 195 (1) 442-8.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 19931015
Last Updated on STN: 19970203
Entered Medline: 19930928

L10 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 96065959 MEDLINE
DOCUMENT NUMBER: 96065959 PubMed ID: 7477934
TITLE: Increased **expression** and subcellular translocation of the mitogen activated protein kinase kinase and mitogen-activated protein kinase in Alzheimer's disease.
AUTHOR: Arendt T; Holzer M; Grossmann A; Zedlick D; Bruckner M K
CORPORATE SOURCE: Department of Neurochemistry, Paul Flechsig Institute of Brain Research, Leipzig, Germany.
SOURCE: NEUROSCIENCE, (1995 Sep) 68 (1) 5-18.
Journal code: 7605074. ISSN: 0306-4522.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 20000303
Entered Medline: 19951130

AB The sequential activation of the mitogen-activated protein kinase kinase and its substrate, the mitogen-activated protein kinase is involved in a cascade of protein kinases which link a number of cell surface signals to intracellular changes in enzyme activity and gene **expression**. In vitro, mitogen-activated protein kinase is able to phosphorylate the microtubule-associated protein tau at Ser-Pro and Thr-Pro sites, thereby generating abnormally hyperphosphorylated tau species that are similar to paired helical filament-tau found in Alzheimer's disease. In the present study, we analysed the levels of immunoreactive mitogen-activated protein kinase kinase and mitogen-activated protein kinase in the temporal cortex (area 22) of patients with Alzheimer's disease by means of enzyme-linked immuno-sorbent assays and compared these changes with the content of abnormally phosphorylated paired helical filament-tau. The levels of immunochemically detected mitogen-activated protein kinase kinase and mitogen-activated protein kinase were both increased in Alzheimer's disease by between 35 and 40% compared with age-matched controls. Elevation of mitogen-activated protein kinase kinase was most pronounced during early **stages** of **Alzheimer**'s disease and was inversely related to the tissue content of abnormally phosphorylated paired helical filament-tau. Pronounced immunoreactivity of mitogen-activated protein kinase kinase and mitogen-activated protein kinase was present in both tangle bearing neurons and unaffected neurons of the temporal cortex. Immunoreactive neurons were most often localized in the direct vicinity of neuritic plaques. In Alzheimer's disease, the subcellular distribution of mitogen-activated protein kinase kinase and mitogen-activated protein kinase showed a striking translocation from the cytoplasmic to the nuclear compartment. It is suggested that the activation of the mitogen-activated protein kinase cascade which appears to be an early feature of Alzheimer's disease might be critically involved in self-stimulating processes of neurodegeneration and aberrant repair under these conditions.